

CLAIMS

1. A spatially delayed-release oral dosage form suitable for oral administration to a mammal, comprising sertraline or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier,
5 which dosage form, following ingestion by said mammal, releases not more than 10% of the sertraline contained therein into said mammal's stomach, and which effects immediate release of the remaining sertraline contained therein after having passed into said mammal's small intestine.
2. A dosage form as defined in claim 1, which is pH-triggered.
- 10 3. A dosage form as defined in claim 2, comprising an immediate-release core coated with a material comprising a polymer that is substantially impermeable to sertraline at the pH of the stomach, but which is permeable to sertraline at the pH of the small intestine.
4. A dosage form as defined in claim 3, wherein said polymer is selected
15 from cellulose acetate phthalate, polyvinylacetate phthalate, hydroxypropylmethyl-cellulose phthalate, cellulose acetate trimellitate, anionic acrylic copolymers of methacrylic acid and methylmethacrylate, and copolymers comprising acrylic acid and at least one acrylic acid ester.
5. A dosage form as defined in claim 3, wherein said core is
20 multiparticulate.
6. A dosage form as defined in claim 3, wherein said core is a tablet.
7. A dosage form as defined in claim 3, wherein said core is a capsule.
8. A dosage form as defined in claim 7, in the form of a gelatin capsule coated with a polymer that is substantially impermeable to sertraline at the pH of the
25 stomach, but that is permeable to sertraline at the pH of the small intestine.
9. A dosage form as defined in claim 1, which is enzyme-triggered.
10. A dosage form as defined in claim 9, comprising:
an immediate-release core comprising sertraline and a pharmaceutically acceptable carrier;
30 a membrane surrounding said core, wherein said membrane is fabricated from a microporous hydrophobic material; and
a hydrophobic liquid entrained within the pores of said membrane, said hydrophobic liquid being substantially impermeable to water and sertraline, but

capable of changing, through enzymatic degradation, so that said membrane becomes substantially permeable to water and sertraline when said dosage form moves into the small intestine.

11. A dosage form as defined in claim 9, wherein said core is a tablet.
- 5 12. A dosage form as defined in claim 9, wherein said core is a multiparticulate.
13. A dosage form as defined in claim 1, wherein said mammal is a human.
14. A pH-triggered delayed release dosage form suitable for oral
10 administration to a mammal, comprising (1) an immediate-release core comprising sertraline or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier, and (2) a pH-sensitive coating surrounding said core,
which dosage form, when dissolution tested in vitro,
releases not more than 10% of its incorporated sertraline in 2 hours in 750 ml
15 of 0.1 N HCl,
and which, following said 2 hours, effects immediate release of its remaining sertraline in a liter of 0.05 M sodium phosphate buffer, pH 6.8, containing 1% polysorbate 80.
15. A dosage form as defined in claim 14, comprising an immediate-
20 release core coated with a polymer that is substantially impermeable to sertraline in said acid but which is permeable to sertraline in said buffer.
16. A dosage form as defined in claim 15, wherein said polymer is selected from cellulose acetate phthalate, polyvinylacetate phthalate, hydroxypropylmethylcellulose phthalate, cellulose acetate trimellitate, anionic acrylic
25 copolymers of methacrylic acid and methylmethacrylate, and copolymers comprising acrylic acid and at least one acrylic acid ester.
17. A dosage form as defined in claim 15, wherein said core is multiparticulate.
18. A dosage form as defined in claim 15, wherein said core is a tablet.
- 30 19. A dosage form as defined in claim 15, wherein said core is a capsule.
20. A dosage form as defined in claim 19, in the form of a gelatin capsule coated with a polymer that is substantially impermeable to sertraline in said acid, but that is permeable to sertraline in said buffer.

21. An enzyme-triggered delayed release dosage form suitable for oral administration to a mammal, comprising (1) an immediate-release core comprising sertraline or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier, and (2) an enzymatically degradable coating surrounding said core,
- 5 which dosage form, when dissolution tested in vitro, releases not more than 10% of its incorporated sertraline in 2 hours in 750 ml of 0.1 N HCl,
- and which, following said 2 hours, effects immediate release of its remaining sertraline in a liter of 0.05 M sodium phosphate buffer, pH 6.8, containing 1% polysorbate 80, in the presence of an enzyme suitable for enzymatically degrading said coating.
22. A dosage form as defined in claim 21, wherein said core is a tablet.
23. A dosage form as defined in claim 21, wherein said core is
- 15 multiparticulate.
24. A dosage form as defined in claim 22, comprising:
a core comprising sertraline and a pharmaceutically acceptable carrier;
a membrane surrounding said core, wherein said membrane is fabricated from a microporous hydrophobic material;
- 20 a hydrophobic liquid entrained within the pores of said membrane, said hydrophobic liquid being substantially impermeable to water and sertraline, but capable of changing, through enzymatic degradation, so that said membrane becomes permeable to water and sertraline in said buffer.
25. A dosage form as defined in claim 24, wherein said core further comprises at least one osmagent.
26. A dosage form as defined in claim 21, wherein said mammal is a human.
27. A temporally delayed dosage form suitable for oral administration to a mammal, comprising (1) an immediate release core comprising sertraline or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier
- 30 and (2) a coating surrounding said core,
which dosage form, following ingestion by said mammal,

releases substantially no sertraline during a first period of about 10 minutes,
releases not more than 10% of the sertraline contained therein during a
second period lasting up to 2 hours following said first period,
and then effects immediate release of the remaining sertraline contained
5 therein.

28. A dosage form as defined in claim 27, wherein said core is a tablet.

29. A dosage form as defined in claim 27, wherein said core is
multiparticulate.

30. A dosage form as defined in claim 28, wherein said tablet is coated
10 with a water-soluble or water-disintegrable coating.

31. A dosage form as defined in claim 29, wherein said multiparticulate is
coated with a water-soluble or water-disintegrable coating.

32. A dosage form as defined in claim 27, in the form of a gelatin capsule
coated with a water-soluble or water-disintegrable coating.

15 33. A dosage form as defined in claim 27, wherein said mammal is a
human.

34. A temporally delayed dosage form suitable for administration to a
mammal, comprising (1) an immediate-release core comprising sertraline or a
pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier
20 and (2) a coating surrounding said core,

which dosage form, when dissolution tested in vitro in a USP-2 apparatus
containing 900 ml of acetic acid/acetate buffer, pH 4.0, which is 0.075 M in NaCl,
releases substantially no sertraline during a first period of about 10 minutes,
releases not more than 10% of the sertraline contained therein during a
25 second period lasting up to 2 hours following said first period,
and which then effects immediate release of the remaining sertraline
contained therein following said second period.

35. A dosage form as defined in claim 34, wherein said core is a tablet.

36. A dosage form as defined in claim 34, wherein said core is
30 multiparticulate.

37. A dosage form as defined in claim 35, wherein said tablet is coated
with a water-soluble or water-disintegrable coating.

*Luclulere
Succinax*

00300000 000700

38. A dosage form as defined in claim 36, wherein said multiparticulate is coated with a water-soluble or water-disintegrable coating.

39. A dosage form as defined in claim 34, in the form of a gelatin capsule coated with a water-soluble or water-disintegrable coating.

5 40. A dosage form as defined in claim 34, wherein said mammal is a human.

41. A delayed-release dosage form suitable for oral administration to a mammal; comprising sertraline or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier, said dosage form exhibiting, *in vivo*, a sertraline plasma T_{max} which is shorter than T_{max} determined after ingestion of an equal amount of sertraline in an immediate release dosage form.

42. A dosage form as defined in claim 41, wherein T_{max} determined with said delayed release dosage form is at least 0.5-hour shorter than T_{max} determined with said immediate release dosage form.

15 43. A dosage form as defined in claim 41, wherein T_{\max} determined with said delayed release dosage form is at least 1hr shorter than T_{\max} determined with said immediate release dosage form.

44. A dosage form as defined in claim 41, wherein said mammal is a human.

20 45. A dosage form as defined in claim 41, which is spatially delayed.

46. A dosage form as defined in claim 41, which is temporally delayed.

47. A dosage form as defined in claim 41, wherein said shortened T_{max} is determined as the average T_{max} from dosing at least 12 normal healthy human subjects in a cross-over study in which said immediate release dosage form is an immediate release tablet.

48. A method for treating a psychiatric illness, premature ejaculation, chemical dependency, premenstrual dysphoric disorder, or obesity, comprising administering to a mammal in need of such treatment, including a human patient, a therapeutically effective amount of sertraline in a delayed-release oral dosage form as defined in claim 1.

49. A method for treating a psychiatric illness, premature ejaculation, chemical dependency, premenstrual dysphoric disorder, or obesity, comprising administering to a mammal in need of such treatment, including a human patient, a

50. A method for treating a psychiatric illness, premature ejaculation, chemical dependency, premenstrual dysphoric disorder, or obesity, comprising
5 administering to a mammal in need of such treatment, including a human patient, a therapeutically effective amount of sertraline in a delayed-release oral dosage form as defined in claim 21.

10

15

20